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A New olefin Derivative from *Ficus esquiroliana* Levl.

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Abstract: A new olefins derivative, ficuole A (**1**) and two known compounds (**2**−**3**) were obtained from the ethyl acetate extract of the *Ficus esquiroliana Levl*. The structures were elucidated using comprehensive spectroscopic methods, and the absolute configurations were defined by comparing the observed optical rotation with the standard values. All compounds were tested for α-glucosidase inhibitory activities. Compounds **1** and **3** against α-glucosidase with the IC_{50} values of 876.5 and 934.6 μM, respectively.

Keywords: *Ficus esquiroliana Levl*; olefins derivative; α-glucosidase activity.

1. Plant Source

The stems of *Ficus esquiroliana Levl* were collected from Haikou, Hainan Province, China, in July 2022, and identified by Prof. Bin Zhang, College of Food and Pharmacy, Zhejiang Ocean University. A voucher specimen (No. ZOU 20220711) has been deposited at, College of Food and Pharmacy, Zhejiang Ocean University.

2. Previous Studies

Ficus esquiroliana Levl. belongs to *Moraceaes* genus of Ficus. In China, *F. esquiroliana*. a species of subtropical tree, is mainly distributed in Hainan, Guangxi, Guangdong, Fujian, and Taiwan [1]. The roots and bark of *F. esquiroliana* are used as a traditional Chinese medicine drug to treat uterine prolapse, rectal prolapse, diarrhea, and other illnesses. [2]. Plants of the genus Ficus comprise exceptional pharmacological activities which have been used traditionally against an array of human and animal diseases related to digestive, respiratory, endocrine, reproductive systems and also a cure for gastrointestinal and urinary tract infections [3-4]. In our research for new bioactive natural compounds from traditional medicinal plants, a new olefins derivative, ficuole A (**1**), along with two known compounds, (6*R*,7*E*, 9*S*)-9-hydroxy-4,7-megastigmadien-3-one (**2**)[5] and blumenol A (**3**)[6] were isolated from the stems of *F. esquiroliana.* (Figure 1.). Herein, we report the isolation, structure elucidation, and inhibitory activity against α-glucosidase of these compounds.

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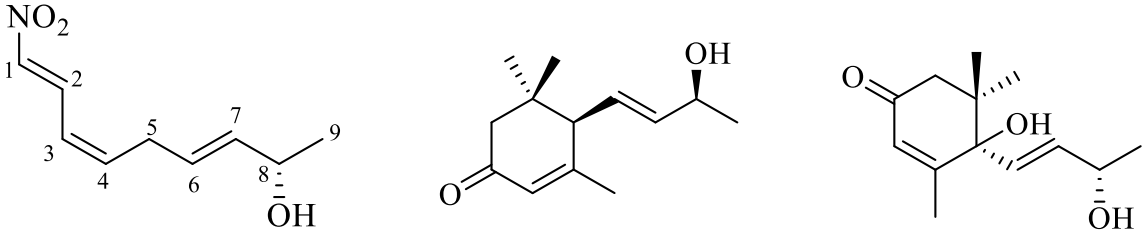
3. Present Study

The air-dried and powdered *F. esquiroliana* plant material (2.0 kg) was extracted three times with 75% ethanol (30 L) at room temperature for 3 days each time. After concentration under reduced pressure, the water-soluble residue was sequentially partitioned with petroleum ether (PE) and ethyl acetate (EtOAc). The resulting fractions were then fractionated to yield 120 g of EtOAc extract, 90 g of PE extract, and 150 g of the aqueous layer. The PE was subjected to silica gel column chromatography (CC) to give five fractions (Frs. 1−5). Frs. 3 (12 g) was further subjected to CC chromatography (PE-EtOAc, 20:1 to 1:1) to yield three fractions (3a–3c). Compounds **1** (6.3 mg) and **2** (7.8 mg) separated from Fr. 3c via by being purified using semi-preparative HPLC (80% MeOH/H_2O). Compound **3** (5.4 mg) was separated from Fr. 3b via by semi-preparative HPLC (60% CH_3CN/H_2O).

*Ficuole A **(1)**:* yellow oiliness; $[\alpha]^{24}_D$ +16.2 (*c* 0.1, CH_3OH); UV (CH_3OH) λ_{max}: 210 nm, 260 nm; IR ν_{max} 3737 (—O—H), 3030 (=C—H), 1645 (C=C), 1029 (C—O) cm^{-1}; ^1H and ^{13}C NMR data see Table 1; HRESIMS (*m/z* 184.0968 $[M+H]^+$, calcd. for 184.0970).

α-Glucosidase Activity Assays: The colorimetric assay for *α*-glucosidase activity was performed as described, with acarbose serving as the reference compound. Acarbose was used as the positive control with an IC_{50} of 893.2 μM. The reaction mixture for *α*-glucosidase inhibitory activity should include 20 μL of compounds **1**-**3** in DMSO (final concentrations of 0.2, 0.05 mg/mL), 10 μL of *α*-glucosidase (1 U/mL), 50 μL of phosphate buffer (pH 6.8), 20 μL of a 2.5 mmol/L substrate solution (p-nitrophenyl-α-D-glucopyranoside), and a final volume of 100 μL. The plates were incubated at 37°C for 15 minutes, then 150 μL was added. The blank and negative control was test by the method. The inhibition rates (%) $=[(OD_{control} - OD_{control\ blank}) - (OD_{test} - OD_{test\ blank})]/(OD_{control\ blank} - OD_{control\ blank}) \times 100\%$. IC_{50} values of the sample were calculated using the IC_{50} calculative software [7,8].



1 **2** **3**

Figure 1. Structures of compounds **1**-**3**

Compound **1** was obtained as yellow oiliness, Its molecular formula was established as $C_9H_{13}NO_3$ (4 degrees of unsaturation) by HRESIMS data (*m/z* 184.0968 $[M+H]^+$, calcd. for 184.0970). The ^1H NMR spectral data (Table 1) of **1** displayed six olefinic proton signals at δ_H 5.82 (d, *J* = 15.2 Hz, H-1), 7.20 (dd, *J* = 15.2, 10.6 Hz, H-2), 6.26 (t, *J* = 10.6 Hz, H-3), 6.11 (m, H-4), 5.42 (m, H-6) and 5.50 (dd, *J* = 17.6, 10.8 Hz, H-7), one methylene signal at δ_H 2.99 (t, *J* = 6.8 Hz, H-5), one oxygenated methine signal at δ_H 4.60 (m, H-8), and one methyl signal at δ_H 1.20 (d, *J* = 6.4 Hz, H-9). The ^{13}C NMR and DEPT-135 data (Table 1) showed 10 resonances, including o six olefinic carbons at δ_C 122.8 (C-1), 145.4 (C-2), 130.1 (C-3), 142.0 (C-4), 127.0 (C-6) and 136.7 (C-7), one methylene carbon at δ_C 31.8 (C-5), one oxygenated methine group at δ_C 64.3 (C-8), and one methyl carbons at δ_C 23.9 (C-9). The ^1H-^1H COSY ((Fig. 2) correlations from H-2 to H-1/3, H-4 to H-3/5, H-6 to H-5/7 and H-8 to H-7/9, combined with the HMBC correlations from H-2 to C-1/4, indicated the structure of **1** as Figure 1. The *E*-configurations of the two double bonds were determined from the coupling constants

of $J_{1,2}$ = 15.2 Hz $J_{6,7}$ = 17.6 Hz. The *Z*-configurations of the one double bond were determined from the coupling constants of $J_{4,5}$ = 10.6 Hz. The absolute configuration of **1** only holding one chiral center at C-8 was determined as *S*-configuration by lactic acid fragments ($[\alpha]^{24}_D$ +2.6), compared with that of standard noniacid B ($[\alpha]^{24}_D$ +11.4). Thus, compound **1** was identified as a new olefins derivative and we named it as ficuole A.

Table 1. ^{1}H (400 MHz) and ^{13}C NMR (100 MHz) spectroscopic data of compound **1**

position	**1** (in CD_3OD)	
	δ_H	δ_C
1	5.82 (1H, d, *J* = 15.2 Hz)	122.8
2	7.20 (1H, dd, *J* = 15.2, 10.6 Hz)	145.4
3	6.26 (1H, t, *J* = 10.6 Hz)	130.1
4	6.11 (1H, m)	142.0
5	2.99 (2H, t, *J* = 6.8 Hz)	31.8
6	5.42 (1H, m)	127.0
7	5.50 (1H, dd, *J* = 17.6, 10.8 Hz)	136.7
8	4.60 (1H, m)	64.3
9	1.20 (3H, d, *J* = 6.4 Hz)	23.9

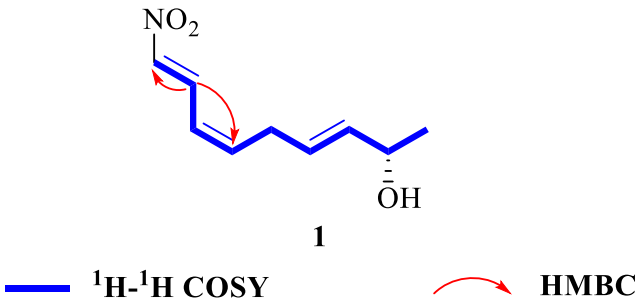


Figure 2. Key ^{1}H-^{1}H COSY and HMBC correlations of **1**.

All compounds were tested for α-glucosidase inhibitory activity (**table 2**.) Compounds **1** and **3** activity against α-glucosidase with the IC_{50} values of 876.5 and 934.6 μM, respectively (positive control acarbose, IC_{50} = 893.2 μM).

Table 2. The inhibitory activity against α-glucosidase for **1** and **3**.

Compounds	**IC_{50} (μM)**
1	876.5
3	9346
Acarbose[a]	893.2

[a]Positive control.

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Supporting Information

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